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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,445	11/20/2003	Dirk Johannes Schaefer	24741-1532	6648

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EXAMINER	
NAFF, DAVID M	
ART UNIT	**PAPER NUMBER**
1657	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/716,445	SCHAEFER ET AL.	
	Examiner	Art Unit	
	David M. Naff	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,8,9,12,13 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-6, 8, 9, 12, 13 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment of 1/4/07 amended claim 39.

Claims examined on the merits are 1, 4-6, 8, 9, 12, 13 and 39, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1, 4-6, 8, 9, 12, 13 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are confusing and unclear by claim 1 requiring a bone substitute comprising components a), b) and c) since after component c) is formed this is the only component present. Components a) and b) form component c), and components a) and b) no longer exist as separate components after component c) is formed. The claim should require the bone substitute to comprise the setting matrix and specify how the setting matrix is formed using components a) and b).

In c) of claim 1, "setting" is uncertain as to meaning and scope. The physical phenomena that constitutes "setting" is uncertain.

Claims 8 and 9 are unclear as to where in claim 1 the cells are present.

In claim 39, bridging lines 4 and 5, the claim is unclear as to steps that constitute treating the cells with a fibrinogen solution and a thrombin solution. To be clear and consistent with the

specification, the claim should require mixing the cells with a fibrinogen solution and then with a thrombin solution to form the form the soft matrix material.

Response to Arguments

The amendment argues that the bone substitute of claim 1 requires the three components recited in the claim. However, this is not the case since after the components are combined to form the bone substitute, the components no longer exist as separate components as claimed. The components exist as claimed only prior to being combined in a process of making the bone substitute. Additionally, requiring cells in b) is confusing since the cells have already been required in a). It is suggested the bone substitute of claim 1 be claimed as a product-by-process claim reciting process steps using components of claim 1 to produce the bone substitute.

It is recognized as urged in the amendment that claim 8 requires additional cells. However, it is unclear where in the components of claim 1 and other preceding claims the additional cells are present.

Claim Rejections - 35 USC § 103

Claims 1, 4-6, 8, 9, 12, 13 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robey et al (5,914,121) in view of Costantino et al (document A08 on 1449 of 11/20/03) and Long et al (5,972,703).

The claims are drawn to a bone substitute containing a soft matrix formed by mixing osteoblasts or precursors thereof with a fibrinogen solution and a thrombin solution, and a setting matrix

formed by mixing the soft matrix with a setting material comprising an aqueous solution of non-ceramic hydroxyapatite cement.

Robey et la disclose preparation of human bone *in vivo* by implanting a composition containing cells, ceramic powder containing hydroxyapatite and fibrin. For example, see claims 1-6.

Costantino et al disclose implanting a composition containing hydroxyapatite that sets *in vivo* for bone replacement.

Long et al disclose (col 13, lines 30-35) combining fibrinogen and thrombin to produce a fibrin clot. The capacity of osteoblasts to produce proteolytic enzymes that lyse the clot is overcome by using epsilon-amino caproic acid (col 13, lines 36-40). Cells that differentiate into osteoblasts are used to treat bone disorders. The cells can be cultivated in the presence of collagen, fibrinogen and fibrin (col 6, lines 40-45).

It would have been obvious to replace the ceramic powder of Robey et al with the hydroxyapatite composition suggested by Costantino et al to obtain its setting function *in vivo*. Long et al would have suggested combining fibrinogen and thrombin to form fibrin by disclosing forming a fibrin clot by mixing fibrinogen and thrombin. Long et al would have further suggested adding aminocaproic acid as in claim 4 to prevent osteoblasts from lysing the clot. Since Long et al use cells that differentiate into osteoblasts to form bone, it would have been obvious to include osteoblasts or precursors thereof in the composition of Robey et al.

Response to Arguments

Contrary to the argument in the amendment, the references establish a prima facie case of obviousness since the references suggest that a bone substitute will be obtained when combining the components of claim 1. The bone substitute of the present invention is merely a combination of components where the combination is merely the sum of the parts due to each component functioning as would have been expected from its function when not in the combination.

The amendment argues that Robey et al do not disclose living cells where at least some of the cells are osteoblasts or precursors thereof. However, as set forth in the rejection, Long et al use cells that differentiate into osteoblasts to form bone, and it would have been obvious to include osteoblasts or precursors thereof in the composition of Robey et al. The rejection is not based on Robey et al alone, and the invention becomes when the references are considered together as a whole. Similarly, Costantino et al is applied with other references. The composition of Costantino et al sets in vivo, and it would have been obvious to replace the ceramic powder of Robey et al with the hydroxyapatite composition suggested by Costantino et al to obtain its setting function *in vivo*. The rejection is not based on modifying Costantino et al, but on modifying Robey et al. Fibrin functioning a support for cells would have been obvious from Long et al, and the composition of Robey et al contains fibrin. While Long et al does not disclose a bone substitute, a bone substitute is suggested by Robey et al, as well as Costantino et al. While claim 39 defines

the bone substitute in terms of an apparatus and process steps of making the bone substitute, the apparatus and process steps do not produce a bone substitute different than would have been obvious from the references applied above.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David M. Naff
Primary Examiner
Art Unit 1657

DMN
4/2/07